(FILE 'HOME' ENTERED AT 14:48:21 ON 02 SEP 1999)

INDEX 'ADISALERTS, ADISINSIGHT, AGRICOLA, AIDSLINE, ANABSTR, AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, CABA, CANCERLIT,

CAPLUS, CEABA, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE,

DRUGB, DRUGLAUNCH, DRUGMONOG2, DRUGNL, ...' ENTERED AT 14:48:27 ON 02 SEP 1999 SEA (ALLOGENEIC OR SYNGENEIC) AND (TUMOR OR CANCER) AND

VACCIN?

- FILE ADISALERTS 10
- FILE ADISINSIGHT 9
- FILE AIDSLINE 4
- FILE BIOBUSINESS 2
- FILE BIOSIS 54
- FILE BIOTECHABS
- FILE BIOTECHDS 7
- FILE CANCERLIT 146
- FILE CAPLUS 47
- FILE DDFB
- FILE DDFU 19
- FILE DRUGB 2
- FILE DRUGNL 3
- FILE DRUGU
- 46
- 139 FILE EMBASE
 - 2 FILE IFIPAT
 - FILE JICST-EPLUS
- FILE LIFESCI 29
- FILE MEDLINE 98
- FILE PHIN 1
- 75 FILE PROMT
- FILE SCISEARCH 56
- FILE TOXLINE 21
- FILE TOXLIT 9
- FILE USPATFULL 316
 - FILE WPIDS
 - FILE WPINDEX

QUE (ALLOGENEIC OR SYNGENEIC) AND (TUMOR OR CANCER) AND T.1

VACCIN?

L2 Α

L3

FILE 'USPATFULL, CANCERLIT, EMBASE, MEDLINE, PROMT, SCISEARCH, BIOSIS, CAPLUS, DRUGU, LIFESCI, TOXLINE, ADISALERTS, ADISINSIGHT, TOXLIT, BIOTECHDS, AIDSLINE, JICST-EPLUS, DRUGNL, BIOBUSINESS, DRUGB, IFIPAT, PHIN' ENTERED AT 14:50:46 ON 02 SEP 1999 1080 S (ALLOGENEIC OR SYNGENEIC) AND (TUMOR OR CANCER) AND VACCIN?

282 S L2 AND VACCIN? (10W) ADJUVANT?

175 DUP REM L3 (107 DUPLICATES REMOVED)

137 S L3 AND CELL(25W) VACCIN?

94 DUP REM L5 (43 DUPLICATES REMOVED)

1 S L3 AND BERD, D?/AU

E BERD, D?/AU

E BERD, DAVID/AU

Serial No: 08/957,691 Page 15

Art Unit: 1642

melanoma tumor cell membranes with BCG which were used to treat skin clinic patient's at the second University of Vienna (page 658, col 2, para 4, the relevant sentence is underlined and is translated as "At the second University of Vienna's skin clinic, patients in Stage IIb were treated with autologous tumor cell membrane preparations with BCG. The reference teaches as disclosed above but does not teach the autologous tumor cell membrane preparation derived from DNP conjugated melanoma cells.

```
ANSWER 22 OF 24 ADISALERTS COPYRIGHT 1999 (ADIS)
     1989:8381 ADISALERTS
ΑN
     800592148
DN
    Clinical responses with active specific intralymphatic immunotherapy for
тT
     cancer - a phase I-II trial
     ADIS TITLE: Cancer: treatment.; Autologous tumour cell
     vaccines
     Wiseman Cl; Rao V S; Kennedy P S; Presant C A; Smith J D; et al
ΑIJ
     Los Angeles Oncologic Institute, Los Angeles, California, USA; St.
CS
Vincent
     Medical Center, Los Angeles, California, USA
     Western Journal of Medicine (Sep 1, 1989), Vol. 151, pp. 283-288
SO
     (Clinical study)
DТ
     Cancer Chemotherapy (Summary): Alert no. 1, 1990
RE
FS
     Summary
LА
     English
WC
     392
TX
     Purpose:
     Intralymphatic inoculation of autologous, irradiated
     tumour cells has increased immunological responses in
     breast and renal cancer and has raised numbers of
     circulating CD4+ lymphocytes. In this study cyclophosphamide pretreatment
     was investigated as a possible inhibitor of suppressor cell activity,
     while the effects of incubation of cells with cholesteryl hemisuccinate,
     with the intent of increasing tumour cell-surface immunogenicity
     by reducing membrane-lipid microviscosity was also examined. In this
phase
     I-II study, the efficacy of intralymphatic immunisation was studied in
     patients with advanced cancer, usually with pulmonary or
     intra-abdominal metastases.
     Author comments:
     Objective regressions were found in 7 of 32 patients, 5 of whom had
     undergone previous chemotherapy. '. . . those very ill patients all had
     tumors for which effective or even palliative therapy is marginal . . . '.
     'The role of cyclophosphamide and of pretreatment of the tumor
     cells with cholesteryl hemisuccinate is still unclear.' 'This process did
     not amplify the response rate in our study. The incidence of clinical
     responses is not meaningfully different among the three series: 3 of 13
     (23%) in series 1, 2 of 7 (29%) in series 2, and 2 of 12 (17) in series
     3. '
     'Our experience suggests that the method of intralymphatic immunotherapy
     is reasonably safe and technically feasible.'
     Study details:
     Design: multicentre, open
     Features: patients were treated with autologous, cryopreserved,
irradiated
     tumour cells which were injected directly into the lymphatic
     system via cannulation of a dorsal pedal lymphatic channel
     Control: drug combination comparison
     Subjects:
     Type: patients
     No: 32
     Groups: 3
     Age: 26-78 (median 48) years
     Sex: 8 female & 24 male
     Characteristics:
     11 patients received no previous treatment
     Concomitant medication:
     IM triethylperazine, 10-15mg prior to cyclophosphamide dose
```

	Drug table:			
		Dose	Route Frequen	ncy Duration
		10-15 x 10 sup(6)	ILy q2-4w	4-24 weeks
	days prior to vaccine)	300 mg/m sup(2)		4-24 weeks
	Results table:			
		Group 1 (n=13)	Group 2 (n=7)	Group 3
	Complete remission Partial remission Mixed response Stable disease Time to progression (weeks) Survival (weeks) Overall median survival =	1 (lung) 0 2 (melanoma, colon) 2 (colon) 4-32 6-300	0) 1 (colon) 1 (melanoma) 4-68 10-169	1 (melanoma) 1 (sarcoma) 0 4-25 6-59
SIDE	Side effects table:			
	Side effects (patients)			
	Wound infection Difficult cannulatio	3	- -	_ _
PNO GNO CT	32			
L4 AN DN TI AU SO	ANSWER 23 OF 24 CANCERLIT 79805339 CANCERLIT 79805339 INDUCTION OF CUTANEOUS DHR TO IRRADIATED AUTOLOGOUS TUMOR CELLS IN INOPERABLE BREAST CANCER. Adler A; Stein J A; Czernobilsky B Non-serial, (1977). Prevention and Detection of Cancer. Part I. Prevention. Vol. 1. Etiology. Proceedings of the Third International Symposium on Detection and Prevention of Cancer held 26 April - 1 May			
1976	New York NY. Nieburgs HE, ed. New York, Marcel Dekker, Inc., 1193 pp., 1977.			
DT FS LA EM AB	Book; (MONOGRAPH) CATH English 197910 Autologous irradiated tumor cell vaccine (I-TCV) was prepared from biopsy specimens of breast cancer from 1 man and 22 women. Six patients had distant metastases; 17 had locally a inoperable tumors and no evidence of metastases. Six areas near lymph nodes were injected id with a mixture of I-TCV (5 x 10(5)			
and	individualized doses of BCG. Unmixed I-TCV (10(7) cells) was injected			
into degr	the center of the rosette. Immunotherapy (ImT) was given 1x/wk. Strong delayed cutaneous hypersensitivity (DCH) reaction to I-TCV, identical DCH reactions to I-TCV/BCG, were elicited in all 17 inoperable patient after 2-6 wk of ImT. Max reactivity was seen after 6-9 wk. A lesser			

of DCH developed in 2/6 patients with metastases. Follow-up times were

2-8

mo, with booster doses (1x/mo) of I-TCV. Two patients needed additional boosters of I-TCV/BCG to maintain their DCH reactions to I-TCV. Suspensions of normal irradiated autologous skin or WBC elicited little

or

no DCH. DCH reactions to nonirradiated autologous tumor cells and I-TCV were identical in 6/6 patients tested. Two inoperable patients showed a flare-up reaction after 4 wk of ImT, simultaneously with the first signs of DCH. These reactions proceeded to central necrosis. One of these patients was given radiotherapy (3,000 rads) before the fifth and last dose of I-TCV/BCG. The bulk of the tumor regressed. During the last 4 mo of the 8-mo observation period, the patient had a recurrent syndrome (every 3-4 wk) of fever, chills, malaise, and inflammatory necrosis of microscopic tumor foci around, but not within, the grossly visible tumor. ImT may favorably alter the host-tumor balance only if the tumor is of microscopic size, which would explain the absence of clinical tumor regression in these patients with large tumors. ImT may be more effective against micrometastases in postmastectomy patients. (5 Refs)